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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,611	03/22/2004	Mary Collins	01997.043200.	2470

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FITZPATRICK CELLA (WYETH)
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-3800

EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,611	COLLINS ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-15,17-36 and 38-49* is/are pending in the application.

4a) Of the above claim(s) *20-28 and 41-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-15, 17-19, 29-36 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/23/08 has been entered.

Status of Application/Amendments/claims

2. Applicant's amendment filed 12/23/08 is acknowledged. Claims 2, 16, and 37 are cancelled. Claims 1, 3-6, 17, and 29-35 are amended. Claims 1, 3-15, 17-36, and 38-49 are pending in this application. Claims 20-28 and 41-49 are withdrawn without traverse (the response filed 8/23/06) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 1, 3-15, 17-19, 29-36 and 38-40 are under examination with respect to IFN-1α/β in this office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

5. Applicant's arguments filed on 12/23/08 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Maintained

In view of the amendment filed on 12/23/08, the following rejections are maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-15, 17-19, 29-36 and 38-40 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing production of IL-10 and decreasing INF-γ IL-1α, IL-2, IL-6, IL-18 and increasing T cell proliferation in an EAE animal model by administration of the IL-21 polypeptide of SEQ ID NO:2 to decrease the severity of symptoms in MS that are regulated by inappropriate cytokine production, does not reasonably provide enablement for suppressing, reducing, delaying or ameliorating a symptom of multiple sclerosis associated with an IL-10 deficiency or increased IFN-γ by administering to a subject all of the agonists of IL-21/IL-21R as in claim 1 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record.

On p. 13-16 of the response, Applicant argues that amended claims are enabled because the specification provides support for treating or ameliorating MS or a symptome thereof based on the EAE mouse model by the claimed molecules. Applicant argues that the instant claims are enabled for the full scope of the claimed invention

because the specification teaches human and murine IL-21 polypeptides, agonsitic IL-21 polypetides, a human IL-21 polypeptide with a deletion of 8 amino acid residues, a fusion protein containing aa 1-122 of SEQ ID NO:2 and an amino acid sequence encoded by a region of SEQ ID NO:1 that encodes a mature human IL-21 polypeptides in paragraphs [0053], [0073-0082], [0067] and [0072]. Applicant argues that the specification teaches amino acid sequences, fragments and variants for making an agonistic anti-IL-21R antibody in pargraphs [0094-0111] & [0050]. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the recitation of "a human or murine IL-21 polypeptide" and the recitation of "a human or murine IL-21R polypeptide" encompass fragments and variants derived from the recited IL-21 and IL-21R polypeptides. However, the specification fails to provide sufficient guidance as to how to make the claimed genus of IL-21 or IL-21R polypeptides.Thus, a skilled artisan cannot contemplate whether all of IL-21 polypeptides that include variants and fragments can be used in treating or ameliorating a symptom of MS.

In addition, although screening for an agonistic anti-IL-21R antibody that is generated from a defined sequence is routine, the claims are not limited to an antibody raised against a specific defined sequence of IL-21R because IL-21R encompasses structurally undefined variants. The specification fails to teach what specific structures and sequences are requried for generating agonistic anti-IL-21R antibodies since the IL-21R polypeptide is not limited to a single amino acid sequence but also encompasses variants and structurally and functionally undefined polypeptides. It is unpredictable

whether all of IL-21R variants and undefined sequences derived from IL-21R polypeptides can generate an agonistic anti-IL-21R antibody.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, it is unpredictable whether the changes can still maintain activity of the wild type of IL-21 polypeptides and whether all of variants or fragments derived from the wild type IL-21R polypeptide can generate an agonistic anti-IL-21R antibody. Thus, the experimentation left to those skilled in the art is extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed invention as currently claimed without further undue experimentation.

Note that

"The 'predictability or lack thereof' in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971)" See MPEP § 2164.03.

7. Claims 1, 29-30, 32-36 and 38-40 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is maintained for the reasons made of record.

On p. 17 of the response, Applicant argues that the rejection has been overcome because the claims have been amended to recite a human IL-21 polypeptide, a murine IL-21 polypeptide, an agonistic anti-human IL-21R antibody, an agonistic anti-murine IL-21R, an antigen-binding fragment of an agonistic anti-human IL-21R antibody and an antigen-binding fragment of an agonistic anti-murine IL-21R antibody. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the specification only teaches an IL-21 polypeptide comprising the amino acid sequence of SEQ ID NO:2 or comprising the amino acid sequence at least 95% identical to SEQ ID NO:2, and the agonistic antibodies generated from the full length wild type amino acid sequence of IL-21R. However, the claims are not limited to the IL-21 polypeptides and agonsitic antibodies as set forth above. As previously made of record, based on the specification (on p.18-20), the recitation of "a IL-21 polypeptide" in the instant claims is not limited to the amino acid sequence of SEQ ID NO:2 or 95% identity to SEQ ID NO:2 because the specification defines "an IL-21 polypeptide" as including fragments of IL-21 and homologues with 30-95% identity to SEQ ID NO:2. However, the specification fails to teach what common structures and amino acid sequences are requried for the claimed genus of IL-21 polypeptides that include fragments and variants and thus can be used in the claimed method.

In addition, the specification fails to limit an IL-21R polypeptide and also fails to teach what sequence is required for generating an agonistic anti-IL-21R antibody. Thus, Applicant was not reasonably in possession of the "claimed genus of human or murine IL-21 polypeptides" and is also not in possesion of "the claimed genus of anti-human or

murine IL-21R antibody and the antigen-binding fragments thereof" and thus Applicant is also not in possession of the claimed method using these claimed genera. Note that

A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119 F.3 at 1568, 43 USPQ2d at 1406. See also *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen Inc. v.Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle &Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-19 and 34-40 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for the reasons made of record.

On p. 17-18 of the response, Applicant argues that a skilled artisan would know the metes and bounds of the claims because the specification states that "IL-10 parameter" is qualitative of quantitative information about IL-10 levels or activity at paragraphs [0014] & [0028]. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the specification only describes examples to assay or evaluate IL-10 activity but fails to limit what specific number or parameter and activity of IL-10 are. Thus, it is unclear to a skilled artisan what parameter and activity of IL-10 are within the scope of the claims and thereby to be

used to measure and determine the efficacy of the treatment. According, the rejection of claims 17-19 and 34-40 under 35 USC 112-2nd paragraph as being indefinite is maintained.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1,3-4, 9-12, 14 and 29-34 stand rejected under 35 U.S.C. 102 (e) as being anticipated by Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006). The rejection is maintained for the reasons made of record.

On p.19-20 of the response, Applicant argues that the '272 patent does not anticipate the claimed method and does not provide an enabling disclosure for the claimed method because the '272 patent teaches a wide range of diseases arising from defects in the immune system and does not specify whether an IL-21 agonist, an IL-21 antagosts or both can be used. Applicant argues that the '272 patent does not teach the regulatory relationship among IL-21, IL10 and IFN-r because the '272 patent fails to indicate how IL-21 is related to IL-10 and/or IFN-g in the complex network of immune

dysfunction. Applicant argues that the '272 patent does not teach a method of treating or ameliorting MS asscoiated with an IL-10 deficiency or increased IFN-γ in patients. Applicant further cites *Verdegaal Bros. v. Union Oil Co.of California* and *In re Hoeksema* in support of the arguments. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the '272 patent is enabling for the instant claims because the '272 patent discloses the claimed method of treating MS using IL-21 and an issued US patent is a reference containing an "enabling disclosure" that the public was in possession of the claimed invention before the date of invention. In *In re Donhue*, the court held that

"A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985)." See MPEP 2121.01 [R3].

The examiner asserts that the '272 patent does teach the claimed method of supressing or ameliorating MS symptoms by IL-21 polypeptides regardless of whether the IL-21 polypeptide is an agonist or antagonist, because the '272 patent teaches the same active step (i.e.administration of IL-21 as claimed) and the same material (i.e. IL-21 polypeptide), and the same patient population (i.e. patients with MS). The '272 patent teaches a therapeutic use of IL-21 (ZALPHA11 ligand) in several immunological disorders including multiple sclerosis as recited in instant claims 1, 3-4, 9-12 and 29-34 (see col. 42, lines 9-31; col.192-198, claims 1-21, in particular).

In addition, the '272 patent teaches that IL-21 enhances proliferation of CD4+ T cells, CD8+ cytotoxicity T cells and Natural killer cells and also teaches that IL-21

enhances regulating production of cytokines such as increasing IL-10 or decreasing IFN-γ to treat immunological disorders mediated by cellular immunity as recited in instant claims 1, 29, 34 (see col.99-102, examples 41-42). The limitation of "suppressing or ameliorating a symptom of MS or MS associated with an IL-10 deficiency or increased IFN-γ" would be an inherent result of administration of IL-21 because IL-21 enhanes secretion of IL-10 and decreases IFN-γ and thereby reverses the condition of IL-10 deficiency and increased IFN-γ in MS. Thus, the '272 patent anticipates the claimed method as recited in instant claims.

On p. 21 of the response, Applicant argues that the examiner has not satisfied the required burden to show the claimed method is inherently disclosed in the '272 patent and cites *Metabolite Labs, Inc. v. Lab. Corp. of Am. Holdings* from MPEP 2112 in support of the arguments. Applicant argues that '272 patent does not specify whether an agonist or antagonist of zalpha1 ligand should be used for specific disorders. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record, the examiner has made a prima facie case to establish that the '272 patent discloses the claimed method. The '272 patent does teach that IL-21 enhances proliferation of $CD4^+$ T cells, $CD8^+$ cytotoxicity T cells and Natural killer cells and also enhances regulating production of cytokines such as increasing IL-10 decreasing IFN-γ to treat immunological disorders mediated by cellular immunity as in instant claims 1, 29, 34 (see col.99-102, examples 41-42). The limitation of "ameliorating a symptom of MS or MS associated with an IL-10 deficiency or

increased IFN-γ" would be an inherent result of regulating immune responses of T cell proliferation and production of cytokines by administration of IL-21 (i.e. an agonist of the IL-21 receptor by definition) as recited in instant claims 1-4, 9-12, 29-31 and 34 because the '272 patent teaches the same active steps of administration of IL-21, the same material (i.e. IL-21) and the same patient population as claimed.

Regardless of whether zalpha1 ligand is an agonist or antagonist, zalpha1 ligand disclosed by the '272 patent is identical to the instant IL-21 polypeptide comprising the amino acid sequence of instant SEQ ID NO:2. In addition, the '272 patent teaches treatment of MS with zalpha1 ligand, which is identical to the claimed method because the patient population, the active steps and the material used in the claimed method are the same. In addition, as previously made of record, as long as the material, active step and patient population are identical in both the claimed method and the '272 patent's method, the limitations of "enhancing secretion of IL-10 and decreasing IFN-γ by IL-21" are inherent results occurring in the patients as evidenced by Wurster.

In addition, note that no other active steps are recited in the claimed method as in instant claims 1,3-4, 9-12, 14 and 29-34. The limitation of ameliorating a symptom of MS associated with an IL-10 deficiency or increased IFN-γ would be an inherent result of administration of IL-21 because IL-21 enhances secretion of IL-10 and decreases IFN-γ and thereby reverses the condition of IL-10 deficiency and increased IFN-γ in MS, which is the immune responses of T cell proliferation and production of cytokines regulated by IL-21 as evidenced by Wurster. Note that

"The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the

discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342,1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). " See MPEP § 2112.01 [R-3].

Furthermore, Applicant fails to show that both of the claimed method and the '272 patent that use the same material and the same step in the same patient population would result in different effects.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1,3-15,17-19, and 29-34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006) in view of Carter et al. (US20030108549A, published Jun 12, 2003, priority date Oct 4, 2001) and Kawai et al.

(Cell Immunol. 1996. 171:262-8). The rejection is maintained for the reasons made of record.

On p. 22-23 of the response, Applicant argues that the '272 patent does not teach the limitations of claims1,3-4, 9-12, 14 and 29-34 because the '272 patent does not teach the modulation of IL-10 or IFN-r by IL-21 or an IL-21/IL-21R agonist would be useful to treat or ameliorate MS or its symptoms. Applicant argues that the combination of the '272 patent with the '549 publication and Kawai does not render the claimed method obvious. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, the '272 patent does teach the limitation of the claims 1, 3-4, 9-12, 14 and 29-34 as set forth above in section of the 102(e) rejection in paragraph 9. Although the '272 patent does not teach an agonistic anti-IL-21 antibody and an anti-inflammatory agent, the '549 publication teaches an agonistic anti-IL-21R antibody as recited in instant claims 1 and 5-6 (see p. 3 [0023], p.5 [0041]) and also teaches the use of a combination of anti-inflammatory agent including IFN-1α/β and an IL-21/IL21R agonist to treat T cell-mediated diseases such as tumor as it relates to claims 7-8 (see p.3 [0024], p.5 [0039], [0040], [0208]). In addition, the '549 publication teaches that an IL-21/IL21R agonist enhances T cell proliferation and cytokine regulation, which relates to ameliorating a symptom of MS associated with cytokines (IL-10 and IFN-γ).

Although the '272 patent and the'549 publication do not teach injection of IL-21 agonists into the CNS as recited in instant claims 13-15, Kawai teaches administering monoclonal antibodies that are against LFA-1 and ICAM-1 in an EAE rat model (a MS

animal model) by intracerebroventricular and intrathecal administration routes. Thus, the claimed method is obvious over the applied references.

11. Claims 1,3-15,17-19,29-36 and 38-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Novak et al. (US Patent No. 6605272, issued Aug 12, 2003, priority date Mar 9, 1999, as cited in IDS submitted May 23,2006), Carter et al. (US20030108549A, published Jun 12, 2003, priority date Oct 4, 2001) and Kawai et al. (Cell Immunol. 1996. 171:262-8) as applied in claims 1-15, 29-34 above and further in view of Beebe et al. (Cytokine & Growth Factor Rev. 2002. 13: 403-12 as in IDS submitted on 05/23/06). The rejection is maintained for the reasons made of record.

On p. 23 of the response, Applicant argues that the '272 patent does not teach the limitations of claims1,3-4, 9-12, 14 and 29-34 because the '272 patent does not teach the modulation of IL-10 or IFN-r by IL-21 or an IL-21/IL-21R agonist would be useful to treat or ameliorate MS or its symptoms. Thus, Applicant argues that the '272 patent in combination with the '549 publication,Kawai and Beebe does not render the claimed method obvious. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as set forth above in section of the 102 (e) rejection in paragraph 9, the '272 patent does teach the limitation of the claims 1, 3-15,17-19, and 29-34. Although the '272 patent, the '549 publication and Kawai do not teach evaluating the level of IL-10 in patients with MS, Beebe teaches that the level of IL-10 is low in patients with MS. Thus, it would have been obvious to a skilled artisan to ameliorate a symptom

of MS regulated by inappropriate production of IL-10 and IFN-γ by incorporating the Beebe's teachings of to measure/monitor the levels of IL-10 in MS patients while practicing the claimed method of the '272 patent, and '549 publication and Kawai because the level of IL-10 is low in MS and EAE, and the level of IL-10 increases after a successful treatment of MS patients.

Conclusion

12. NO CLAIM IS ALLOWED.

13. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
March 05, 2009

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649